PCT/GB98/02151 WO 99/05175 60

## **CLAIMS**

25

A monoclonal or polyclonal antibody or equivalent ligand with reactivity against 1. an anti-TCR VB antibody, for use as a pharmaceutical or as a diagnostic agent.

- An antibody with reactivity against an anti-TCR VB antibody, for use as a 2. pharmaceutical or as a diagnostic agent.
  - An antibody or equivalent ligand according to either of claims 1 or 2 with 3. reactivity against both an anti-TCR Vβ antibody and a GPI-linked TCR Vβ chain, for use as a pharmaceutical or as a diagnostic agent.
- An antibody or equivalent ligand according to any one of claims 1 to 3 with 4. reactivity against any one of the following compounds: a phospholipid, a phospholipid 10 glycan, single stranded DNA and double stranded DNA, for use as a pharmaceutical or as a diagnostic agent.
  - An antibody according to any one of the preceding claims which is a 5. monoclonal antibody, for use as a pharmaceutical or as a diagnostic agent.
- An antibody or equivalent ligand according to any preceding claim which is of 15 6. vertebrate or invertebrate origin, for use as a pharmaceutical or as a diagnostic agent.
  - An antibody or equivalent ligand according to any preceding claim that is 7. derived from B cells immortalised by Epstein-Barr virus transformation or other methods using B cells obtained from healthy or diseased humans or animals.
- An antibody or equivalent ligand according to any one of the preceding claims 20 8. which is isolated by passing body fluid from animals or humans down an antigen conjugated column, for use as a pharmaceutical or as a diagnostic agent.
  - An antibody or equivalent ligand according to claim 8 wherein said animals or 9. humans are immunised with antigen, are diseased or have been manipulated by drug or by diet so as to develop a disease, for use as a pharmaceutical or as a diagnostic agent.
  - An antibody or equivalent ligand according to any one of the preceding claims 10. which is chemically-modified, bound to a biological or synthetic substance, or which is

conjugated to an enzyme, an indicator compound, a drug, a toxin or a radioactive label, for use as a pharmaceutical or as a diagnostic agent.

- 11. Use of an antibody or equivalent ligand according to any one of the preceding claims in the manufacture of a medicament for the treatment of IDDM, NIDDM, or organ or non-organ specific autoimmune disease, cardiovascular disease, cancer cachexia and cancer or any other diseases where anti-phospholipid antibodies and/or hyperinsulinaemia and insulin resistance are present.
- 12. A peptide, oligopeptide, polypeptide or protein that is bound by a monoclonal or polyclonal antibody or equivalent ligand according to any one of claims 1 to 10, which is not an anti-TCR  $V\beta$  antibody, for use as a pharmaceutical or as a diagnostic agent.

10

15

- 13. Use of a peptide, oligopeptide, polypeptide or protein that is bound by a monoclonal or polyclonal antibody or equivalent ligand according to any one of claims 1 to 10, which is not an anti-TCR V $\beta$  antibody, in the manufacture of a medicament for the treatment of IDDM, NIDDM, or organ or non-organ specific autoimmune disease, cardiovascular disease, cancer cachexia and cancer or any other diseases where antiphospholipid antibodies and/or hyperinsulinaemia and insulin resistance are present.
- 14. A peptide, oligopeptide, polypeptide or protein comprising the sequence of ESRP1.
- 15. A peptide, oligopeptide, polypeptide or protein according to claim 14, for use as a pharmaceutical or as a diagnostic agent.
  - 16. Use of a peptide, oligopeptide, polypeptide or protein according to either of claims 14 or 15 in the manufacture of a medicament for the treatment of IDDM, NIDDM, or organ or non-organ specific autoimmune disease, cardiovascular disease, cancer cachexia and cancer or any other diseases where anti-phospholipid antibodies and/or hyperinsulinaemia and insulin resistance are present.
  - 17. A cDNA, RNA or genomic DNA sequence encoding a monoclonal or polyclonal antibody or equivalent ligand with reactivity against an anti-TCR Vβ antibody or encoding a peptide, oligopeptide, polypeptide or protein that is bound by a monoclonal or polyclonal antibody or equivalent ligand with reactivity against an anti-

TCR VB antibody, which is not an anti-TCR VB antibody for use as a pharmaceutical or as a diagnostic agent.

- A cDNA, RNA or genomic DNA sequence encoding ESRP1. 18.
- 19. A bacteriophage clone comprising a cDNA, RNA or genomic DNA sequence according to claim 18.
  - A biologically functional plasmid or viral vector comprising a cDNA, RNA or 20. genomic DNA sequence according to claim 19.
- A bacteriophage clone, biologically functional plasmid or viral vector 21. comprising a cDNA, RNA or genomic DNA sequence according to any one of claims 18-20, for use as a pharmaceutical or as a diagnostic agent.
  - A host cell that is stably transformed or transfected with a plasmid or vector 22. according to either of claims 20 or 21.
  - A method for detection of a naturally-occurring autoantibody, comprising 23. contacting a blood, plasma or serum sample or other body fluid with a monoclonal or polyclonal antibody or equivalent ligand according to any one of claims 1 to 10 and with target molecules and assessing the amount of said naturally-occurring autoantibody that binds specifically to the target molecules.
  - The method of claim 23 wherein said antibody, fragment thereof or functional 24. equivalent is labelled according to claim 10 so that the labelled antibody or equivalent ligand competes with the autoantibodies for the target molecules to form complexes and whereby the amount of label bound in said complexes is inversely proportional to the concentration of autoantibodies present in said sample.
  - The method of claim 24, wherein said antibody or equivalent ligand is labelled 25. with an enzyme so that the formation of said complexes inhibits or inactivates the activity of said enzyme and whereby the degree of inhibition or activation is inversely proportional to the concentration of autoantibodies that are present in said sample.
    - A method according to either of claims 24 or 25, wherein said target molecules 26. are bound to an enzyme linked to a substrate such that binding of antibody to the target

molecules activates the enzyme and causes a colour change that is measurable spectrophotometrically.

- 27. A method according to any one of claims 23-26, wherein said target molecules are bound to an enzyme linked to a substrate and are present on a dipstick which can be contacted with said sample.
- 28. A method according to any one of claims 24-27, wherein said target molecule is an anti-TCR V $\beta$  polyclonal or monoclonal immunoglobulin molecule or any part thereof that identifies at least one epitope on T cell receptor V $\beta$  chains in humans or any animal species.
- 29. A method of treatment of IDDM, NIDDM, or organ or non-organ specific autoimmune disease, cardiovascular disease, cancer cachexia and cancer or any other diseases where anti-phospholipid antibodies and/or hyperinsulinaemia and insulin resistance are present involving appying to a patient a monoclonal or polyclonal antibody or equivalent ligand with reactivity against an anti-TCR Vβ antibody or a peptide, oligopeptide, polypeptide or protein that is bound by a monoclonal or polyclonal antibody or equivalent ligand with reactivity against an anti-TCR Vβ antibody, which is not an anti-TCR Vβ antibody, in an effective amount, optionally in conjunction with a pharmaceutically-acceptable carrier.